

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 14542-PCT		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/IB2004/001040		International filing date (day/month/year) 05.04.2004	Priority date (day/month/year) 04.04.2003	
International Patent Classification (IPC) or national classification and IPC C12N15/09, C12N15/15, C12P21/02, C12N9/64				
Applicant UNIVERSITE DE LAUSANNE et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 5 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 04.02.2005		Date of completion of this report 29.09.2005		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Simm, M.D. Telephone No. +49 89 2399-7411 		

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/001040

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-39 as originally filed

Claims, Numbers

1-38 received on 08.02.2005 with letter of 04.02.2005

Drawings, Sheets

1/15-15/15 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/B2004/001040

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 18-22
because:
 - ☒ the said international application, or the said claims Nos. 18-22 in respect of i.a. relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☒ no international search report has been established for the said claims Nos. 18-22
 - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
 - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
 - ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/001040

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	4,13, 24,27, 37
	No: Claims	1-3,5-12,14-17,23, 25,26,28-36,38
Inventive step (IS)	Yes: Claims	4,13,37
	No: Claims	6,10,11, 24,27
Industrial applicability (IA)	Yes: Claims	1-17,23-38
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/001040

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

Re Item III.

Claims 18-22 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

- 1 The following documents are referred to in this communication:
D1 : US 5 827 662 A (COOPERMAN BARRY ET AL) 27 October 1998 (1998-10-27)
D2 : WO 95/27053 A (UNIV PENNSYLVANIA) 12 October 1995 (1995-10-12)

2 INDEPENDENT CLAIM 1

- 2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

Document D1 (see column 6, lines 48-67, Table I and II and claims 1-6) discloses a method of producing recombinant serine protease inhibitors (antichymotrypsin variants) capable of effectively modulating serine protease activity. The inhibitor comprises a hinge region of a reactive loop which have modified aminoacid sequences (positions 349-368). Kallikrein is mentioned on column 10, lines 5 and 13.

The compositions are specially useful in regulating inflammatory processes related to serine proteases accumulating in cells or tissues: tumour migration is mentioned among others (claim 3).

Similarly, D2 (page 4, first paragraph and page 14, last paragraph) discloses antichymotrypsin analogue shaving aminoacid substitutions at positions 356-361, useful in the treatment of lung inflammation among others.

Thus, in view of D1-D2 the present claim 1 and the dependent claims 2-3,5,7,8,9 are not novel.

3 INDEPENDENT CLAIMS 12,14,16, 17, 23 and 28

These independent claims would be novel and inventive only when referring to a novel and inventive inhibitor protein, because D1-D2 comprise as well the isolated DNA encoding for the recombinant inhibitor protein, the expression vector, the cells, the pharmaceutical compositions (or strong indications), the medical use and the method of producing the inhibitor and diagnostic kits.

Moreover, the subject-matter of dependent claims 15,25,26, 29-36 is as well disclosed in D1-D2 or is common procedure in the field.

- 4 The sequences corresponding to SEQID N° 1-22 are novel. The exact mutations of RSL sequences 16-22 have not been found in the prior art. These specific recombinant ACT inhibitors are in view of the examples of the present application more specific to a targeted serin protease as the wild-type ACT. Thus, specific recombinant ACT inhibitors appear to be inventive.
- 5 Claims 1-3 and 5 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

Claims 1-3 are not supported by the description as required by Article 6 PCT, as its/their scope is broader than justified by the description and drawings. The use of the word "chimeric" in the present invention is not justified, the proteins claimed are not chimeras (two different genes as origin of the protein) but just recombinant variants of ACT.

- 6 The subject-matter of claims 6, 24 and 27 although formally new, would only appear to be inventive when combined with the claims related to novel and inventive inhibitor protein of protease (Art. 33(3) PCT).